

GEMS meeting showcases new genetic research funded by NIEHS

By Eddy Ball

The role of genetic variation in shaping host response to environmental exposures was the focus of the [Genetics and Environmental Mutagenesis Society \(GEMS\)](#) Spring Meeting.

Attendees gathered on April 27 at the U.S. Environmental Protection Agency (EPA) conference center in Research Triangle Park, North Carolina, to learn about new developments in work by four local research groups funded by NIEHS. The featured scientists use systems genetics approaches in mice and flies, and genome-wide association studies (GWAS) in humans, to analyze quantitative traits.

GEMS President and EPA senior scientist Channa Keshava, Ph.D., presented opening remarks before handing the program over to GEMS President-elect and program chair [Stephanie Smith-Roe, Ph.D.](#), a genetic toxicologist with the National Toxicology Program (NTP).

Mice bred for genetic diversity create a more informative model

Smith-Roe introduced retired NTP toxicologist Jef French, Ph.D., who led efforts to use a new mouse model population for improved studies of chemical toxicity. Using the model known as Diversity Outbred (DO) as one component of the [Tox21 program](#), researchers will be able to test chemicals prioritized by high-throughput screening far more effectively than is possible with the traditional approach, which uses one strain of mouse and one strain of rat in a two-year assay.

According to French, the DO mice, which are derived from outcross breeding of 175 Collaborative Cross (CC) pairs, more closely resemble the diversity in human populations compared with the genetic uniformity in traditional lab animal lines (see related [story](#)). “Each [mouse] is genetically different from the others,” he said.

A thematically consistent, but operationally distinct approach, was presented by University of North Carolina at Chapel Hill (UNC) geneticist [Samir Kelada, Ph.D.](#) Kelada is an NIEHS Outstanding New Environmental Scientist awardee who uses the CC mouse model for studying the genetics of environmentally induced airway disease.

Building on well-established paradigms

“Everything old is new again” could easily have been the subtitle of the talk by geneticist [Trudy MacKay, Ph.D.](#), from North Carolina State University. MacKay’s team is working to define the intricate genetic architecture of environmental sensitivity in fruit flies.

Although fruit flies are a long-established model, MacKay’s innovation is an intensive multigenerational inbreeding program involving flies from a very specific location — the Raleigh, North Carolina farmers’ market. In addition to studying gene-environment interactions, the researchers are tracing the interaction networks of common genes. “It turns out to be more complicated than we thought,” she said.

The program concluded with a presentation of results from large-scale human studies by NIEHS molecular epidemiologist [Stephanie London, M.D., Dr.P.H.](#), “Smoking and the Epigenome Across the Lifecourse.” In a landmark [2012 study](#), London’s group used a new, specialized tool for assessing epigenetic modifications from DNA methylation.

The team then conducted GWAS and identified several novel genes specific to tobacco smoke detoxification and other development processes in more than 1,000 pregnant mothers and their offspring from a Norwegian cohort (see [story](#)). Their results were validated in separate studies by other groups, and London’s group is now participating in even larger scale, multicohort studies.

(Eddy Ball is a contract writer for the NIEHS Office of Communications and Public Liaison)



Smith-Roe had reason to smile at the event. “Stephanie has put a wonderful program together,” Keshava told the audience, “and she has also lined up truly excellent speakers.” (Photo courtesy of Steve McCaw)



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French explained that differences between the reactions of genetically uniform and genetically diverse mice can reach orders of magnitude. "It gives us more power," he said of the DO mouse model. (Photo courtesy of Steve McCaw)



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"Where does the variance in response come from?" Kelada asked. Despite their different models, each of the speakers is trying to answer this fundamental question about gene-environment interaction. (Photo courtesy of Steve McCaw)



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With a short tribute by retired NTP toxicologist Mike Shelby, Ph.D., the audience paused to remember the life of Frederick de Serres, Ph.D., who died in December 2014. de Serres hired Shelby as a lab tech in 1967 and helped shape his career. (Photo courtesy of Steve McCaw)



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An NIEHS grantee, MacKay holds an appointment as a distinguished professor and her long list of honors includes election to the National Academy of Sciences, and being named a Fellow of the United Kingdom's Royal Society. (Photo courtesy of Steve McCaw)



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Each of the speakers received a token of appreciation from GEMS. Shown, left to right, are Smith-Roe, London, and Keshava. (Photo courtesy of Steve McCaw)



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Along with active scientists from NIEHS, EPA, and local universities, the audience included retired NTP toxicologist Barbara Shane, Ph.D., left, and retired NIEHS scientist Errol Zeiger, Ph.D., J.D. (Photo courtesy of Steve McCaw)



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Biostatistician David Umbach, Ph.D., center, was among NIEHS scientists in attendance. GWAS studies involve an immense amount of data and routinely include statisticians as co-authors. (Photo courtesy of Steve McCaw)

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